Autonomous Extracellular Matrix Remodeling Controls a Progressive Adaptation in Muscle Stem Cell Regenerative Capacity during Development.

Journal: Cell Rep

Publication Year: 2016

Authors: Matthew Timothy Tierney, Anastasia Gromova, Francesca Boscolo Sesillo, David Sala, Caroline Spenle, Gertraud Orend, Alessandra Sacco

PubMed link: 26904948

Funding Grants: Type III CIRM Stem Cell Research Training Program

Public Summary:
Muscle stem cells (MuSC) are essential for skeletal muscle growth and repair. Although major efforts in recent years have improved our understanding of the molecular pathways regulating their function, the transition of MuSC from development to adulthood is still poorly defined. In this study we show that fetal MuSC more efficiently expand and contribute to muscle repair than adult counterparts. The findings revealed that fetal MuSC possess a remarkable regenerative potential through more efficient expansion, intrinsically regulating their behavior through the selective expression of extracellular matrix proteins to remodel their local microenvironment. The identified components of the fetal MuSC niche could be exploited as novel tools to direct adult muscle stem cell activity towards the immediate or long-term aspects of tissue repair, thus facilitating the development of novel regenerative medicine approaches for muscle wasting diseases.

Scientific Abstract:
Muscle stem cells (MuSCs) exhibit distinct behavior during successive phases of developmental myogenesis. However, how their transition to adulthood is regulated is poorly understood. Here, we show that fetal MuSCs resist progenitor specification and exhibit altered division dynamics, intrinsic features that are progressively lost postnatally. After transplantation, fetal MuSCs expand more efficiently and contribute to muscle repair. Conversely, niche colonization efficiency increases in adulthood, indicating a balance between muscle growth and stem cell pool repopulation. Gene expression profiling identified several extracellular matrix (ECM) molecules preferentially expressed in fetal MuSCs, including tenascin-C, fibronectin, and collagen VI. Loss-of-function experiments confirmed their essential and stage-specific role in regulating MuSC function. Finally, fetal-derived paracrine factors were able to enhance adult MuSC regenerative potential. Together, these findings demonstrate that MuSCs change the way in which they remodel their microenvironment to direct stem cell behavior and support the unique demands of muscle development or repair.